Triethylene Glycol Dimethyl Ether

CAS #112-49-2
Swiss CD-1 mice, at 0.0, 0.25%, 0.5%, 1.0%, in drinking water
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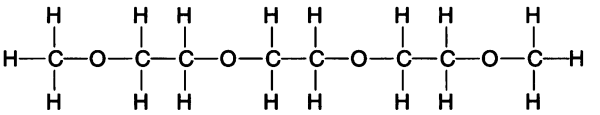
NTIS: PB85150456/AS



Triethylene glycol dimethyl ether (TGDME) was tested in the RACB protocol as part of a larger effort to evaluate a series of glycol ethers and their structural congeners and metabolites (Bossert et al., Fundam Appl Toxicol 18:602–608 [1992]). Previous studies indicated significant prenatal toxicity for TGDME, but reproductive toxicity had not previously been evaluated. Data on body weights, food and water consumption, and clinical signs from the Task 1 dose-range-finding study were used to set doses for the continuous cohabitation phase, Task 2, at 0, 0.25, 0.5, and 1.0% EGDME in the drinking water. In combination with a 30 to 60% consumption increase at the highest concentration, these concentrations produced calculated consumption estimates of approximately 43.8, 87.5, and 175.0 mg/kg/day.

Adult body weights were not changed during Task 2, but at the highest concentration, the number of litters per pair and the number of live pups per litter were reduced by 12 and 50%, respectively. Pup weight adjusted for litter size was reduced at the middle and highest concentrations by 4 and 8%, respectively. Additionally, days between litters were increased from the third litter on at the middle and top dose levels, by 3 to 6 days.

Task 2 was followed by Task 3, a crossover mating to determine the affected sex. This Task re-paired the control and high concentration groups for a week-long mating trial. While all groups showed equal evidence of mating, the group pairing treated females with control males had a 58% reduction in the proportion of females delivering live young. There was an increase in the proportion of dead pups delivered to treated females, and the adjusted pup weight was 6% less than controls.

After these pups were delivered and evaluated, the F_0 mice from the control and 1% TGDME groups were killed and necropsied. There was no treatment-related effect on body weights, but body weight-adjusted liver weight was increased by 17 to 21% in both sexes. The only other effect noted was a 12.5% decrease in female pituitary weight. Epididymal sperm concentration, motility, and abnormal forms were unchanged.

The effects of TGDME on reproduction in a second generation were not evaluated in this study.

In summary, this study found that triethylene glycol dimethyl ether produced developmental toxicity, as indicated by the reduced pup weights, and female reproductive toxicity, manifested by fewer litters in the high dose group in Tasks 2 and 3.

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: **PB85150456/AS**
Chemical: **Triethylene Glycol Dimethyl Ether**
CAS#: **112-49-2**
Mode of exposure: **Drinking water**
Species/strain: **Swiss CD-1 mice**

F_0 generation — Dose concentration →	0.25%	0.5%	1.0%
General toxicity	Male, female	Male, female	Male, female
Body weight	—, —	—, —	—, —
Kidney weight[a]	•	•	•
Liver weight[a]	•	•	↑, ↑
Mortality	•	•	•
Feed consumption	•	•	•
Water consumption	—, —	—, —	↑, —
Clinical signs	—, —	—, —	—, —
Reproductive toxicity			
x̄ litters/pair	—	—	↓
# live pups/litter; pup wt./litter	—, —	—, ↓	↓, ↓
Cumulative days to litter	—	↑	↑
Absolute testis, epididymis weight[a]	•	•	—, —
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	•	—, —
Epidid. sperm parameters (#, motility, morphology)	•	•	—, —, —
Estrous cycle length	•	•	•

Determination of affected sex (crossover)	Male	Female	Both
Dose level	•	1.0%	•

F_1 generation — Dose concentration →	•	•	•
General toxicity	Male, female	Male, female	Male, female
Pup growth to weaning	•	•	•
Mortality	•	•	•
Adult body weight	•	•	•
Kidney weight[a]	•	•	•
Liver weight[a]	•	•	•
Feed consumption	•	•	•
Water consumption	•	•	•
Clinical signs	•	•	•
Reproductive toxicity			
Fertility index	•	•	•
# live pups/litter; pup wt./litter	•	•	•
Absolute testis, epididymis weight[a]	•	•	•
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	•	•
Epidid. sperm parameters (#, motility, morphology)	•	•	•
Estrous cycle length	•	•	•

Summary information	
Affected sex?	**Female**
Study confounders:	**None**
F_1 more sensitive than F_0?	**Unclear**
Postnatal toxicity:	**Unclear**

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change ($p<0.05$); —, —, no change in males or females. [a]Adjusted for body weight.